Biotinidase Deficiency

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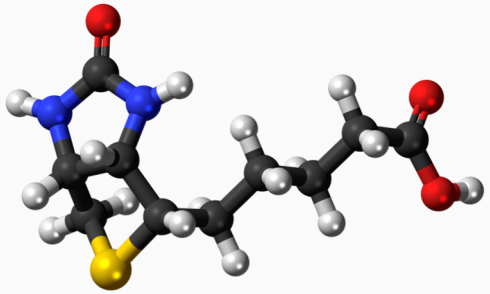

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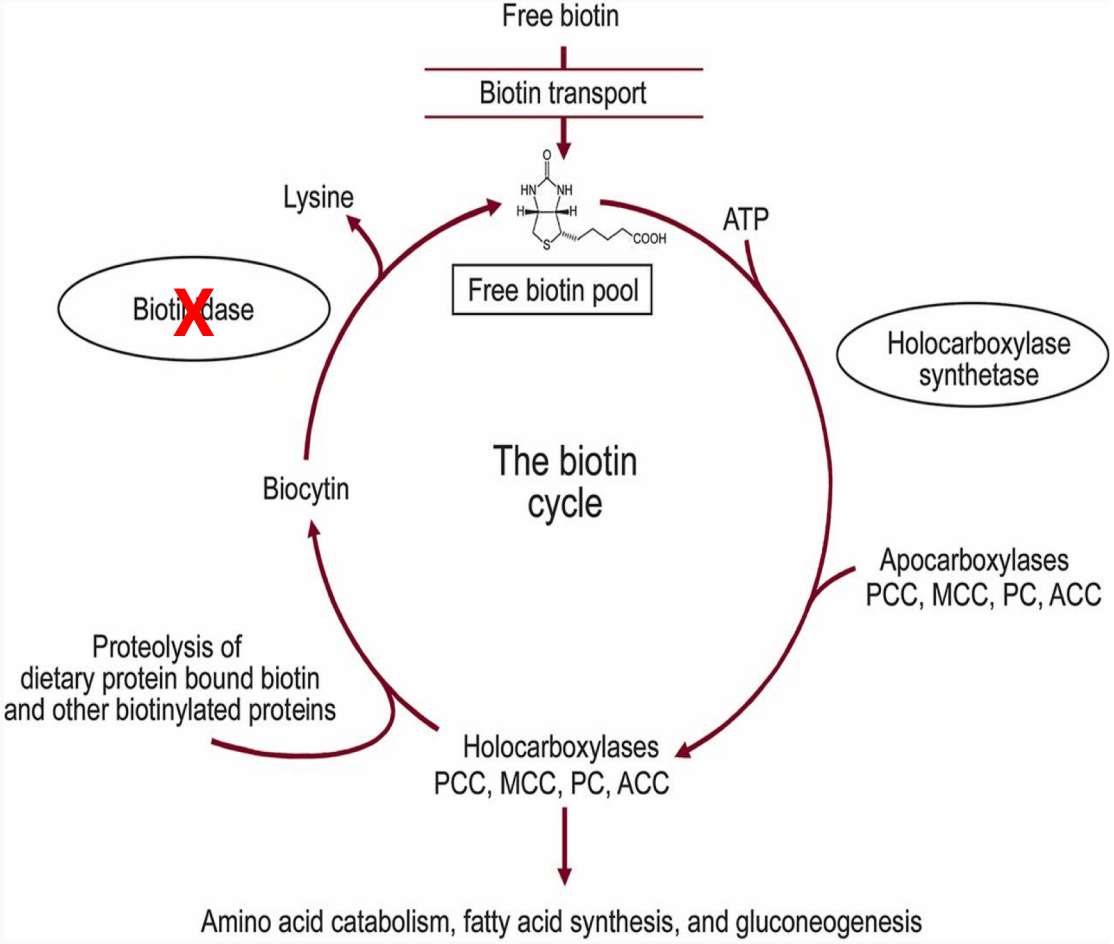
What is biotinidase deficiency?

- Mutation in the biotinidase gene
- Autosomal recessive disease
- Biotinidase, an enzyme, helps (i) capture biotin from the diet, and (ii) recycle existing biotin, for metabolic use during:
  - Glucose synthesis
  - Amino acid breakdown
  - Fatty acid synthesis



Abbreviations used

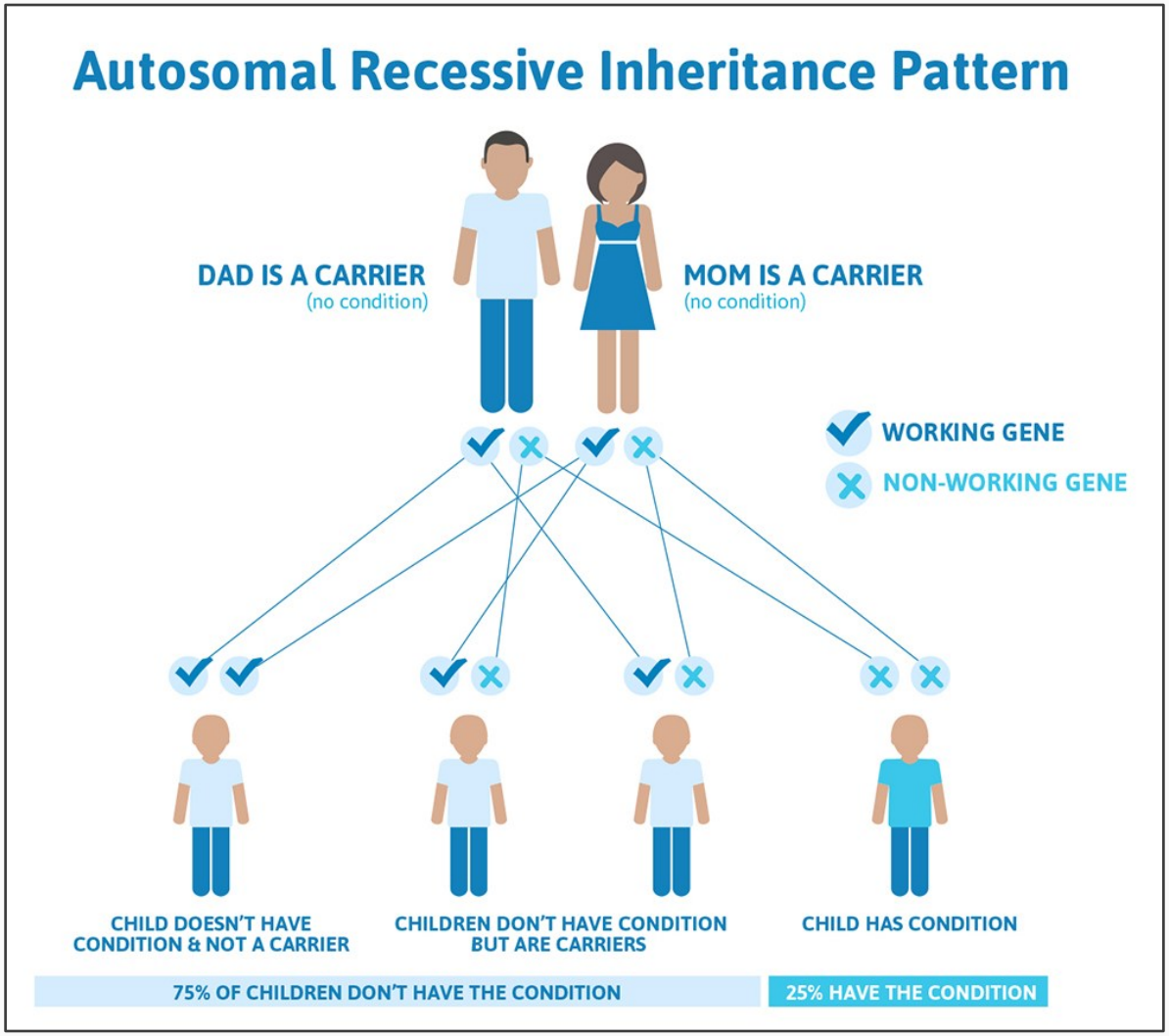
PCC: propionyl-CoA carboxylase; MCC, 3-methylcrotonyl-CoA carboxylase

PC, pyruvate carboxylase; ACC, acetyl-CoA carboxylase

Digital image retrieved 10-09-2019 from

https://cp.neurology.org/content/7/6/518/tab-figures-data

Genetics of biotinidase deficiency



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https://www.geneticsupport.org/genetics-101/inheritance-patterns/autosomal-recessive/

Biotinidase deficiency: Consequences

When biotin is not available for metabolic use,

food cannot be efficiently stored or used as fuel

Food

Biotinidase

Energy

Occurrence

- Occurrence

  - Biotinidase deficiency found in 1/60,000 newborns, albeit to varying levels depending on the mutation

  - Carrier frequency is approximately 1/120

  - Higher occurrence among people of European descent

Symptoms

- Symptoms usually occur within the first few months of life when biotin stores run out
- Many of the symptoms affect the brain and other parts of the nervous system
- Symptoms are due to the buildup of harmful metabolites
- If an individual has partial biotinidase deficiency, they may experience these symptoms but only during an illness, infection, or a time of stress

Symptoms

Many children have early symptoms such as:

1. Seizures
2. Weak muscle tone
3. Trouble breathing

Additional symptoms that develop later:

1. Skin rashes
2. Hair loss
3. Developmental delays
4. Hearing / vision loss
5. Paralysis
6. Death if untreated

Photos of biotinidase deficient patients.

Digital image retrieved 11-11-19 from

https://www.michigan.gov/documents/mdch/Barry_Wolf_Biotinidase_Def_501204_7.pdf

Floppy baby syndrome

Digital image retrieved 11-11-19 from

https://pedsinreview.aappublications.org/content/30/9/e66

Diagnosis

- Newborn screenings - blood test to check biotinidase activity
- Urine tests for elevated levels of 3-hydroxyisovaleric acid and 3-methylcrotonylglycine due to a lack of biotin
  - Urine may smell like cat urine due to elevated levels of certain organic acids
- Prenatal screening via amniotic fluid analysis
- Using family history to estimate an increased probability
- Genetic testing that detect mutations in the biotinidase gene

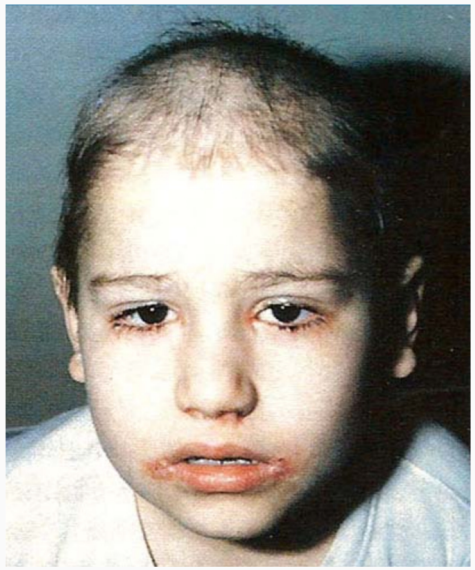
Therapy and Prognosis

- Given early diagnosis and treatment, the long-term prognosis for biotinidase deficiency is excellent and patients typically lead healthy lives

- Lifetime oral biotin
  - 5-10 mg daily dosages (inexpensive)
  - Up to 40 mg/day for severe deficiencies

Digital Image retrieved 11-11-19 from https://www.amazon.com/Natures-Bounty-Supplement-Supports-Healthy/dp/B001115TLM

Biotin treatment: positive clinical outcomes



Before treatment

After treatment

Before and after treatment photos of biotinidase deficient patients.

Digital image retrieved 11-11-19 from

https://www.michigan.gov/documents/mdch/Barry_Wolf_Biotinidase_Def_501204_7.pdf

Dietary intervention

- Dietary measures
  - Avoid raw egg whites because avidin in egg white binds to biotin and prevents its absorption

Support groups

Services include:

- Connection with other patients and families
- Medical advices from specialists
- Information on clinical research and screening
- Advocacy

Logo from Genetic and Rare Diseases Information Center, a resource for those with metabolic diseases. Digital image retrieved 11-11-19 from https://rarediseases.info.nih.gov/about-gard/pages/23/about-gard

Logo from Metabolic Support UK
Digital image retrieved 01-11-20
https://www.metabolicsupportuk.org/

Sources

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Biotinidase Deficiency: Project Team

Name	Project Role
Kyle Hua	Project Leader; Therapy
Lizzie Sawdai	Biochemical features
Jacob Beal	Occurrence and genetics
Lauren Rager	Diagnosis
Tia Renko	Symptoms
Christopher Trent	Prognosis
Ashwin Kalyanakumar	History
Tashiki Nakao	Support
Paul Blasiman	Support